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Feasibility of Atrial Delivery and Tracking of Stem Cells in a Porcine Model

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mass index $48.62 \pm 8.0 \text{ kg/m}^2$ and mean preoperative excess weight $171.28 \pm 52.0 \text{ lbs}$. Median follow-up after LAGB was 63.63 months (range 0.0–162.4) for a total of 4,859 patient-years. During follow-up, 103 patients (11.9%) underwent reoperation for slippage at a median of 54.26 months (range 0.0–160.50) after LAGB. We found a significantly lower weight at rebanding, and at 1, 2, 3, 4 and 5 years after rebanding in patients with slippage compared to their initial weight, and their weight at 1, 2, 3, 4 and 5 years after LAGB. There was a significantly lower excess weight loss failure rate in patients with slippage compared to matching controls (40% vs. 60%, $P=0.0006$) after first year. There were no differences in EWL rate between the two groups after first year. In multivariate analysis only female gender was significantly associated with slippage.

Conclusion: Failure rate of excess weight loss after rebanding for slippage was lower or similar to the failure rate after initial laparoscopic adjustable gastric banding.

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Background: Many patients undergoing open heart surgery have sinus node dysfunction and atrial fibrillation, leading to adverse outcomes. Mesenchymal stem cells (MSC) delivered at the time of surgery may have a reparative effect on atrial tissue, thereby improving sinus node function and reducing or preventing atrial fibrillation. Stem cell delivery to the atrium is entirely unstudied. This is a significant gap in medical research, as atrial disease contributes significantly to health care costs.

Purpose: The purpose of this pilot study is to establish a technique to deliver MSC to the atria through an open-chest model, to assess the safety of this technique, and to evaluate the acute retention of the delivered cells.

Methods: All in vivo animal experimentation was approved by the University of Wisconsin Animal Care and Use Committee and took place in the Cardiovascular Physiology Core Facility at UW-Madison. MSC ($3\text{--}5 \times 10^6$ in $50 \mu\text{l}$ per site) were injected intramyocardially during an open-chest procedure in anesthetized pigs. To track the cells in vivo, MSC were labeled with ^{18}F FDG then visualized at 1 and 6 hours postinjection by PET/CT. Pigs were monitored for intraoperative arrhythmia, bleeding and hypotension.

Results: By gently repositioning the heart, both atria were accessible for the injections. The thickest part of each atrium was isolated and stabilized briefly for the injection using a hemostat. The injected cells were visible by PET/CT 1 and 6 hours postinjection. However, when the MSC were

labeled with $10\text{mCi } ^{18}\text{F}$ FDG, the signal was too high, causing a bloom around the areas of injection. So the dose was lowered to $5\text{mCi } ^{18}\text{F}$ FDG, which resulted in a clear signal at 1 hour in both atria. At 6 hours, the right atrial injection was still easy to read, but the left injection was difficult to resolve from background signal. All injections resulted in cell leakage from the injection site and uptake of the signal into the lungs. However, pulmonary function as measured by SpO_2 and EtCO_2 was unchanged. Intraoperative arrhythmias detected during the injections were caused by manipulation of the heart. No additional arrhythmias were detected. No bleeding or hypotension was observed as a result of the injections.

Conclusion: This pilot study demonstrated that atrial delivery of MSC is feasible and safe in an open-chest porcine model and that MSC are retained for at least 6 hours postinjection. Subsequent studies will determine the ability of MSC to downregulate inflammation, decrease scarring and prevent sinus node dysfunction.

Does the Expression of Ki-67, p16 and COX-2 at Initial Diagnosis of Breast Atypia or Usual Ductal Hyperplasia Predict a Second Clinically Significant Event?

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Background: Women diagnosed with atypical ductal hyperplasia (ADH) or atypical lobular hyperplasia (ALH) have a fivefold increased risk of developing breast cancer. Because ADH/ALH can be precursors or predictive markers of a subsequent clinically significant event (SCSE), i.e. atypia, in situ or invasive carcinoma, the clinical outcome for these patients ranges anywhere from remission to invasive malignancy. Currently we cannot predict which atypical breast lesion is likely to be associated with future cancer, resulting in aggressive management and, possibly, overtreatment. Kerlikowske et al. reported that a combination of three biomarkers (cell cycle regulator p16INK4a, proliferation antigen Ki-67 and stress response enzyme COX-2) predicted risk of progression for ~50% of women diagnosed with ductal carcinoma in situ and treated by lumpectomy alone.

Purpose: To evaluate whether expression levels of p16, Ki-67 and COX-2 predict risk of development of a SCSE in patients initially diagnosed with breast atypia (ADH or ALH) or usual ductal hyperplasia (UDH).

Methods: Patients with an initial diagnosis of pure ADH/ALH were identified by medical record review and the lesion confirmed by a single pathologist blinded